

The Neuroscience of Social interaction

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In the last two decades, researchers have made enormous strides toward understanding the brain. The neural substrates of visual perception, memory, and learning have been investigated in depth, leading to a much greater understanding of the underlying mechanisms involved. In addition, the advent of neuroimaging has made it possible to study neural activity related to mental processes involved in social understanding such as recognizing facial expressions of emotion. In comparison, relatively little is understood about how the brain facilitates, and is influenced by, social interaction and relationships. One reason for this is that neuroscience has historically treated people as isolated units, separate from their social context. This approach perseveres today in large part due to the pragmatics of functional neuroimaging. It is difficult to interact with others while lying supine in a functional magnetic resonance imaging (fMRI) scanner, sitting still under a magnetoencephalography helmet, or while wearing 128 electrodes adhered to one's scalp. However, although research using interactive paradigms is currently sparse, research on social understanding within the individual sheds light on the processes integral to healthy social interaction. Here this literature is summarized followed by a final section highlighting recent progress made towards observing these processes in vivo; during real-time social interaction.

I. Understanding others

Detecting animacy

The first thing a brain must do in any healthy social interaction is detect animacy. Indeed, psychophysical research has shown that our attentional and perceptual systems are uniquely tuned for detecting animate things versus other object types. This step is so obvious as to be overlooked in most analyses of social cognition, but it is critical. If the brain was unable to quickly and efficiently differentiate animate from inanimate objects, time-consuming mental calculations would be wasted attempting to predict the thoughts, feelings, and actions of objects that could not think, feel, or act. The importance of this step is highlighted in ontogenesis. Early in development, the brain begins to cleave the world into animate and inanimate objects. This primary coding scheme allows human beings to devote cognitive resources to understanding, predicting and interacting with the only objects that can understand, predict, and interact in return: animate beings. At birth, infants preferentially track moving human faces. At 3 months, they smile and vocalize more to people than objects and show preferential attention to self-propelled motion; a hallmark of animacy. By 9 months, infants understand that animate beings, not objects, have goal-directed action. And by 18 months infants know that only animate beings have mental states. This incremental trajectory from animacy detection to mentalizing suggests that detecting animacy is a primary milestone of social perception; establishing the neural foundation upon which subsequent social understanding is built. Consistent with this view, the mere interpretation of animacy engages the same neural network known to subserve more advanced social understanding while inanimate interpretations do not (Figure 1).

FIGURE 1. The social brain. Converging evidence points to a network of areas involved in

understanding others. A. This network includes areas associated with biological motion (1, superior temporal sulcus), biological form (6, lateral fusiform gyrus), mentalizing (3, medial prefrontal cortex; 4, posterior cingulate) and affective processing (2, insula; 5, amygdala; *figure adapted from Saxe, 2006*). B. When contextual cues bias an interpretation of animacy (e.g., "ice-skater"), a moving shape engages the social network compared to when the same moving shape is interpreted as inanimate (e.g., "spinning top"). Brain slices depict activity across the network when the same moving shapes were inferred (red) or imagined (orange) as animate rather than inanimate (Wheatley, Milleville & Martin, 2007). Yellow areas were more active for both animate inference and imagery ("conjunction"). Animacy may serve as an initial alert to ready the network for incoming social information. Presumably, the demands of the social situation at hand would then modulate activity within these areas, increasing activity in some areas relative to others (e.g., amygdala for fear recognition).

Counter-intuitively perhaps, the healthy development of ascribing animacy is defined by inaccuracy. Normal children over-attribute animacy to their teddy bears and dolls and a more subtle form of anthropomorphism extends into adulthood. When shown simple animations of interacting shapes, healthy adults impute motives, emotions, even gender. In contrast, anthropomorphism is muted or absent entirely in people with autism spectrum disorders (ASD), in which the most common clinical sign is social interaction impairment. Thus, an over-active ascription of animacy may be an early indicator of a healthy brain tuning itself to the recognition of conspecifics.

Theory of Mind

Perhaps the most important attribute of the social brain is the ability to attribute mental states to others in order to better predict their actions. The underlying assumption -- that behavior is caused by mental states -- has been called taking an 'intentional stance' or 'having a theory of mind' (ToM). ToM is not easily measured by overt behavior and observation. Tests to see whether a child possesses a theory of mind usually involve stories in which false beliefs must be inferred. In one well-known example, a child is shown two dolls: Sally and Ann. Sally has a basket and Ann has a box. The child watches as Sally puts a marble in the basket and leaves. While Sally is gone, "naughty" Ann takes the marble out of the basket and puts it in the box. Then Sally returns. The child is asked: "Where will Sally look for the marble?" (Figure 2). The correct response requires understanding that Ann moved the marble *unbeknownst* to Sally and that Sally thus holds a false belief that the marble is still in the basket. Healthy and IQ-matched Down's syndrome children succeed at this task around the age of 4. Before that time, children have difficulty grasping that a person can believe something decoupled from reality.

FIGURE 2. Theory of Mind tasks. A) The Sally-Ann false belief test uses two dolls, "Sally" and "Anne". Sally has a basket; Anne has a box. Sally places a ball in the basket and leaves. While Sally is gone, Anne takes the ball and puts it in her box. Children are asked where Sally will look for the ball. Around age 4, children understand that Sally can believe something that is false: that the ball is still in the basket (Adapted from Frith & Frith, 1999). B) "Reading the Mind in the Eyes" task is a more advanced test of Theory of Mind for adults. The subject must match up mental state terms to eyes (Baron-Cohen & Cross, 1992). C) Theory of mind stories require inferences about the characters' thoughts and feelings. This paragraph requires second-

order reasoning; the consideration of what one person thinks about another person's thoughts (Happe, 1994).

Autistic individuals have particular difficulty in tasks like these that require taking into account what someone else knows or expects. Children with autism have a failure rate estimated at upwards of 50% on the Sally-Ann task. If the task requires the added difficulty of understanding what a person thinks about *another* person's beliefs or thoughts (i.e., second-order mental state attribution), the failure rate in autistic individuals approaches ceiling. While autistic individuals may develop strategies using non-mentalistic representations to pass some of these tests, difficulty representing another's thoughts is a hallmark of autism that endures throughout the lifespan.

Patients, such as those with autism, provide rich data for researchers attempting to elucidate the neural substrates of mentalizing, the largely automatic process by which we 'read' the mental states of others. Intuitively, if a brain region is dysfunctional in a disorder marked by the inability to mentalize, one can deduce that this region subserves mentalizing in the healthy brain. The story is invariably more complex. Patients with disorders defined by social deficits have concomitant non-social deficits (e.g., motor tics, verbal dysfluencies) with associated neural activity that can mask or obfuscate activity specific to the social domain. However, research with patients and healthy adults has converged on three brain areas that are consistently modulated by tasks requiring the inference of mental states: the temporal poles (TP), posterior superior temporal sulcus (pSTS), and medial prefrontal cortex (mPFC). Healthy adult volunteers recruit these areas when inferring mental states from expressions in photographs,

attributing mental states to animations of geometric shapes, and imputing mental states to characters in cartoons and stories.

Theory of mind: Temporal poles. The temporal pole (TP) is the anterior-most end of the temporal lobe. Based on its proximity and connections to orbitofrontal cortex and the amygdala, it is often considered a paralimbic area. A large white matter tract (the uncinate fasciculus) links the region to the prefrontal cortex and it receives and sends projections to the basal forebrain and three sensory systems (visual, auditory, olfactory). Due to its unusually interconnected nature, the TP is sometimes described as association cortex.

Lesions of the TP in monkeys yield grossly abnormal social behavior. These monkeys neither decode the social signals of their conspecifics appropriately nor produce appropriate social signals themselves. They lose normal emotional attachments to their infants and peers. TP dysfunction in humans, as seen in herpes encephalitis and the temporal-variant of frontal temporal dementia (tv-FTD), also leads to severe socio-emotional deficits including depression, socially inappropriate behavior, and a lack of empathy.

In the intact adult brain, TP activity correlates positively with narrative coherence; the degree to which a story is being communicated in contrast to isolated facts. The temporal poles activate more strongly to sentences than word-strings, to narratives than nonsense, and to more- versus less- coherent stories and appear especially sensitive to narratives of a social nature. Finally, TP cortex appears to play a role in coding personal memories, in particular linking person-specific memories to faces, scenes, and voices. Together, these findings suggest that the role of the temporal pole is to evaluate stimuli in terms of relevant personal narratives or "scripts". These scripts include facts about social situations; the changes in behavior appropriate to changing social demands, and how one's feelings and actions affect the behavior of others in

these situations. These scripts are dynamically updated by personal experience, presumably via connections to the medial temporal lobe memory system. Damage to the temporal poles can impair the ability to use this knowledge. Without the ability to link incoming social information to normative and autobiographical social and contextual knowledge, the social motives and appropriateness of others' behavior are difficult to ascertain. Consistent with this view, patients with TP lesions have particular difficulty predicting how people will behave in social and emotional circumstances even if they know them quite well (e.g., relatives).

Theory of mind: Posterior superior temporal sulcus (pSTS). Numerous studies with human and non-human primates have demonstrated that the superior temporal sulcus is engaged during the perception of biological motion. Activations along the human STS have been noted when healthy participants view videos of people moving, static photographs implying movement, and point-light displays (movies constructed by attaching small lights to a subject's major joints and filming movements in the dark). The posterior extent of STS in particular, appears to be modulated by the kind of articulated, fluid motion associated with living beings in comparison to the rigid, simple motion of inanimate things (e.g., tools). When transcranial magnetic stimulation (TMS) is used to disrupt brain activity in this region, people are selectively impaired in recognizing biological motion in upright (normal) point-light displays. More importantly for the present discussion, this region appears particularly active when motion cues express social information such as intent. Fritz Heider and Mary-Ann Simmel first showed our proclivity to make social inferences from motion in the 1940's with simple cartoons of interacting circles and triangles. These simple, motion cartoons evoked inferences of intent, emotion, gender, and even personality in the human participants. Subsequent research has demonstrated that various types of human motion express emotional, motivational, and

intentional states (e.g., communicative gestures, gaze shifts) and that these motions have been associated with activity in the pSTS. For example, pSTS is activated when participants observe someone moving their eyes. Moreover, this activity is modulated by contextual cues: more activity is elicited in pSTS if an actor moves her eyes away from, rather than towards, a flashing target.

In addition, this region has been associated with the attribution of mental states even in the absence of motion cues (e.g., judgments of trustworthiness). This final point has led some researchers to speculate that there are adjacent but distinct areas within this region of cortex that subserve three processes: recognition of biological motion, recognition of mental states from motion cues, and the ability to mentalize whether or not motion cues are present. The latter ability appears to be associated primarily with the posterior-most portion of the superior temporal sulcus that extends superiorly into the temporo-parietal junction (TPJ). The TPJ has been implicated in perspective-taking and, most recently, how we perceive our own body in space. Abnormal electrical activity in this area in patients creates an out-of-body experience in which patients report looking at their body from above. TMS disruption to this region also produces impairments in the ability to imagine how one's body looks from another's perspective. Thus, this region appears to support mentalizing via biological motion cues to intent and imagining different spatial and mental perspectives from one's own.

Superior temporal sulcus abnormalities have been highly implicated in ASD including decreased gray matter concentration, hypo-perfusion at rest, and abnormal activation during social tasks. STS anatomical and functional anomalies occurring early in brain development have been suggested as the first step in a cascade of neural dysfunction underlying ASD.

Theory of mind: Medial prefrontal cortex. The area of medial prefrontal cortex consistently activated by mentalizing is the most anterior part of the paracingulate cortex, lying anterior to the genu of the corpus callosum (Figure 3). Activity in this anterior region has been associated with the perception of pain and tickling, as well as autobiographical memory and aesthetic judgment. Across these seemingly disparate studies, a common denominator has emerged. Rather than trace the specific content of a sensory experience, mPFC appears to subserve the ability to *attend to* the mental states that give rise to experience. That is, to create an explicit representation of what one thinks or feels *about* X. Recent research suggests that this area is also important for taking the perspective of another person (i.e., “how would you feel if you were person X”). This suggests that being able to represent our own subjective experience relates to the ability to understand the subjective experience of others.

FIGURE 3. Medial prefrontal cortex. Dots are locations of peak activations during tasks when participants monitor their own mental states or attribute mental states to others (Frith & Frith, 1999).

More evidence that medial prefrontal cortex subserves the understanding of another’s intentions comes from research involving communicative actions. Actions intended to communicate meaning to someone else (e.g., pointing to a bottle to request it) activate mPFC more than actions that are non-communicative (e.g., changing a broken light bulb in order to read). Similarly, intentions related to current and foreseen social interactions (e.g., preparing a romantic dinner) yield more mPFC activity than intended actions for solitary purposes. Thus this area appears to be especially tuned to interacting minds rather than minds in isolation.

Research on different types of dementia are consistent with the mPFC playing a key role in social awareness and comportment. Frontal variant frontotemporal dementia (fvFTD) has disproportionate medial prefrontal degeneration compared to other dementias (e.g., Alzheimers) and is associated with striking changes in personality and social behavior. As reported by relatives and care-givers, these patients become more impulsive, emotionally cold and self-centered with a commensurate loss of empathy and insight. Relatedly, they have disproportionately poor performance on tasks that require ToM-related abilities including detecting deception, false beliefs, and faux pas, and are impaired in recognizing mental states conveyed by eye gaze. This poor performance on a variety of ToM tasks stands in contrast to their relatively unimpaired executive functioning abilities (e.g., working memory) and in contrast to other dementias that are not characterized by ventromedial prefrontal damage (e.g., Alzheimer's disease).

Decoding Emotion

Successful social interactions rest not only on understanding what other people are thinking but also on what they are feeling. Knowing when to console, placate, or simply listen quietly is understood largely through decoding a person's nonverbal behavior. Overwhelmingly, this research has focused on the face as the main channel of emotional expression (Figure 4), although, some research has investigated other channels such as bodily movement and prosody.

FIGURE 4. A. Emotional facial expressions¹. In the 1960's, Paul Ekman demonstrated that facial expressions of emotion are universal and thus, presumably, biological in origin as Charles

Darwin once theorized (Ekman & Friesen, 1975). Since Ekman's discovery, photographs of emotional expressions have been widely used in psychological research to understand how people recognize another's emotions. Neuroimaging research has focused on two areas that are involved in emotion recognition. A) The amygdala, known to be involved in fear conditioning, is most active when recognizing fear compared to other facial expressions (Whalen, 1998). B) The anterior insula, associated with taste processing, subserves the recognition of another's disgust (Calder, Lawrence, & Young, 2001).

¹Development of the MacBrain Face Stimulus Set was overseen by Nim Tottenham and supported by the John D. and Catherine T. MacArthur Foundation Research Network on Early Experience and Brain Development

Decoding emotion: Faces, motion, and prosody

Faces yield a wealth of information critical for human survival and well-being. Given this importance, it has been suggested that face perception and recognition hold a privileged status in the human brain. Indeed, face stimuli are associated with robust activity in three regions of cortex: lateral fusiform gyrus, superior temporal sulcus, and the amygdala. Most notably, a portion of the lateral extent of the fusiform gyrus dubbed the Fusiform Face Area (FFA) appears to track the perception and recognition of the structural properties of a face. Lesions to this area can create prosopagnosia: the selective inability to recognize faces in comparison to other objects. However, despite difficulties recognizing even highly familiar faces consciously, prosopagnosic patients can identify people by voice and show a heightened emotional response (skin conductance) to familiar others indicating an unconscious level of recognition. Thus, even when conscious facial recognition fails, other brain regions aid the all-important task of identifying conspecifics in the environment. While the static properties of a face are reliable indicators of personal identity, it is the ability to manipulate these features

dynamically that allows humans to express changing social signals such as emotional, motivational, and intentional states. This dynamic facial information is subserved by a region already discussed in terms of understanding motion cues of intent: superior temporal sulcus.

Dynamic facial and whole-body expressions quickly and reliably convey multiple social cues from boredom to empathy. Often subtle and fleeting, the degree to which these cues are identified and read appropriately is a sign of social intelligence. Converging evidence points to the posterior superior temporal sulcus as a nexus for the perception of biological motion including gaze shifts, mouth movements, and communicative gestures. Most recently, this area has been associated with processing social information conveyed by such movements including a person's intent and emotional state.

When coupled with gestures, affective prosody or 'tone of voice' gives energy to discourse and influences the content and impact of what is said. Indeed, prosody can convey communicative intent more so than the literal meaning of the words employed. The statement "I am so happy for you" could be either literal or ironic as conveyed solely by tone of voice. Prosody can telegraph emotions, motives and motivational states from apathy to flirtation. Although these paralinguistic features are not explicitly taught, learning them is critical for social success.

A series of clinical studies have shown that focal damage to the right hemisphere selectively impairs the production, comprehension and repetition of affective prosody without disrupting the propositional elements of language. In one study, right brain-damaged patients with unilateral retro-Rolandic lesions were markedly impaired on understanding affective prosody when compared to healthy controls or left brain-damaged patients. In a follow-up study, right but not left hemisphere lesions impaired the ability to insert affective variation into verbally

neutral sentences both on request and on a repetition task. Subsequent research has dissociated the neural correlates of affective prosody production from its comprehension. The inability to project emotion into one's speech is associated with damage to the posterior-inferior frontal lobe including the pars opercularis and triangularis, a region similar in location to Broca's area in the left hemisphere. The inability to understand emotion in someone else's speech is associated with damage to the right posterior superior temporal lobe, a region similar in location to Wernicke's area in the left hemisphere. Thus, the functional-anatomic organization of prosody in the right hemisphere may be somewhat similar to the functional-anatomic organization of propositional language in the left hemisphere.

Evidence from patients and neuroimaging studies suggest that the ability to recognize the emotions of animate agents relies on an interconnected web of areas with each area contributing disproportionately to the processing of one or more emotional cues (e.g., facial expression). In addition to responding to a variety of cues, the areas within this network operate at multiple temporal scales from the rapid, coarse processing of salient features to slower, more evaluative processes that incorporate contextual information.

Decoding emotion: Rapid processing

Amygdala. Some responses in the brain to emotional facial expressions are so rapid (< 100ms) that they could not plausibly be based on conscious awareness of the stimulus. This evidence comes from research using event-related potentials that measure the brain's electrical activity at the scalp as well as from studies that present faces so quickly that participants have no conscious awareness of having seen them. One possibility suggested by these studies is that this rapid, nonconscious processing of emotional visual stimuli may occur subcortically,

involving brainstem nuclei such as the superior colliculus as well as the amygdala, a small structure adjacent to the medial temporal lobe.

Consistent with evolutionary pressures, this rapid system appears to respond to all animate stimuli and, moreover, seems to be especially geared to detect threats. Facial expressions that denote threat (anger) and a potentially threatening environment (fear) are associated with a heightened amygdala response relative to stimuli judged to have a more neutral affective valence. Such rapid processing implies a reliance on highly over-learned or innately-specified visual cues. One such marker that has been identified is the eye whites of fearful faces which are notably larger than eye whites associated with other emotions (Whalen et al., 2004). Intriguingly, recent research suggests that the amygdala also responds more to faces deemed untrustworthy. It is unclear whether this activity reflects rapid processing of salient visual markers of untrustworthiness (yet to be identified) or later inferential processing involving higher-level cortical areas, or both.

Consistent with a role of the amygdala in modulating vigilance, abnormal activity in this region yields abnormal levels of anxiety. Hyper-activity within the amygdala is associated with greater anxiety as shown in borderline personality disorder, depression, and severe social phobia. In contrast, hypo-activity in this area is associated with lowered anxiety, increased self-confidence, reduced empathy and the disorder characterized by these symptoms: psychopathy. Although psychopathy is related to amygdala hypoactivity, it is not the case that amygdala damage produces psychopathy. Bilateral amygdala lesions do not appear to impair empathy or social relationships, but rather predict a tendency to be overly trusting and generous. It is likely, therefore, that amygdala damage by itself does not yield poor social interactions and relationships. Rather, these difficulties arise in disrupted connections linking the perceptual

representations from the amygdala with abstract representations of their social and emotional significance.

Decoding emotion: Evaluation of significance

Orbitofrontal cortex (OFC). Linking the perceptual information in facial expressions with their social and emotional significance appears to be largely the domain of the orbitofrontal cortex. The social and emotional significance of a stimulus is evaluated by weighing the current context, personal experience with that stimulus, and its reward value. Unlike the amygdala that is biased towards detecting aversive contingencies very quickly, OFC underlies both positive and negative associations and appears to operate at a timescale more conducive to the evaluation of contextual cues, social norms, and background knowledge. That is, OFC appears to take the perception-based signals coming from the amygdala and evaluate those signals for appropriateness (situational norms, personal history) and their present or potential reward value. It has been suggested that orbitofrontal activity influences the amygdalae via reciprocal connections between the two regions. Such connections have been observed in non-human primates and rats, and is indirectly supported by research on reappraisal. In this research, a perceived threat (e.g., snarling dog) is reappraised to seem non-threatening (e.g., the dog is behind glass). Without the reappraisal, the amygdala is engaged significantly. With reappraisal, OFC is activated and the signal in the amygdala is suppressed. This finding suggests that the initial alert from the amygdala is quelled by the OFC once the threat is reappraised in a non-threatening context. Presumably, the OFC could also increase amygdaloid vigilance to particular stimuli if necessitated by a particular goal or context. The possibility of projections between the OFC and amygdala sounds a general caution against rigidly assigning particular cognitive processes to particular neural structures. It is probable that any single structure

participates in several processes depending on the details of the task, the context, and the time scale involved.

Decoding emotion: Simulation

Somatosensory cortex. One model of emotion processing in the human brain has proposed that recognizing emotions in others relies in part on the observer's simulation of that emotional state (Damasio, 1994). Accordingly, somatosensory cortices which subserve cutaneous, kinesthetic, and visceral sensations may be recruited during emotion recognition. In support of this hypothesis, two somatosensory regions (right parietal and insular cortices) have been associated with recognizing and understanding the emotions of others. Damage to the right ventral parietal cortex has been associated with significantly impaired recognition for multiple emotions as well as impaired touch sensation, suggesting that facial expressions activate somatosensory regions in order to produce inferences about how a person feels. Similarly, the insular cortex, a visceral somatosensory area implicated in taste perception in humans and primates, is activated for the facial expression of disgust. The role of somatosensory cortices in emotion recognition is also supported by anosognosic patients whose reduced activity in these areas is associated with impaired knowledge of their own body state, often accompanied by a flattening of emotion. This overlap of related perceptual and conceptual processes, is consistent with the idea that emotion recognition may depend in part on reactivating circuits that had been involved in the learning of one's own emotional reactions.

Whether such re-activations involve simulating an “as if” emotional state in oneself (i.e., a truly empathic, reenactment leading to the overt experience or “feeling” of the emotion) rather than an entirely covert, unconscious re-activation of information is a matter of debate. It is plausible that a conscious experience or feeling only occurs when it is difficult to understand what someone is feeling otherwise. This would be consistent with the scientific theory that top-

down reconstruction processes continue only as far “backwards” in the processing stream as necessary for comprehension (Kosslyn & Thompson, 2003). Regardless of whether this process is overt or covert, the somatosensory cortices appear to play a role in representing how another person feels, literally.

Social understanding requires recognizing what people are thinking and feeling. Without being able to do so, social interactions become bewildering and patients risk social isolation and withdrawal. While the ability to decode another’s intentions and emotions is necessary for successful social interaction, it is not sufficient. In turn, one must respond appropriately to those social signals. This behavioral component of social interaction relies on understanding when and how to act.

II. Responding to social signals

Self regulation

Ever since Phineas Gage impaled his orbitofrontal cortex with a two-inch thick iron rod, damage to this area of cortex has been associated with impaired social functioning. Like Gage, orbitofrontal-damaged patients are characterized by their lack of social comportment, impulsivity and lack of insight. These deficits appear to stem from an inability to use normative and reward information to regulate their behavior. Intriguingly, recent research suggests that it’s the ability to regulate behavior *in the moment* that is the primary deficit. OFC patients are able to report social norms accurately such as what information is and is not appropriate to disclose to a stranger. Moreover, OFC patients are able to indicate when they were acting inappropriately upon reviewing their behavior on video. Thus, the primary deficit appears to be a lack of self-monitoring in the present moment.

This titration of appropriate responding based on moment-by-moment processing of social information in the environment is consistent with the theory of an OFC-amygdala circuit. That is, the amygdala monitors the environment for biologically relevant cues (e.g., another's emotions) and the OFC tags that information with social or emotional significance based on the present context which then serves to increase or decrease amygdala activity to those cues and so on. This feedback loop not only affords a continual assessment of social information, but also the appropriate generation and suppression of behavioral responses to that information (e.g., whether to laugh or hit someone that made an insulting remark).

Communication pragmatics

Knowing what to say and do based on social cues must be combined with knowing *when and how* to say and do it. Collectively known as communication pragmatics, these rules of turn-taking, intonation (prosodics) and interpersonal distance (proxemics) are learned implicitly over the course of normal social development. How the brain represents this information is not well understood although some clues can be found in patients that lose this understanding after having developed it normally. When such a loss occurs it is typically precipitated by damage to the right hemisphere.

For most people, the right hemisphere (RH) is the nondominant hemisphere for speech and language and yet it is this hemisphere that seems to play an outsized role in understanding when and how to respond during conversation. Correspondingly, patients with right hemisphere damage (RHD) tend to suffer not from aphasia but from an inability to understand the unwritten rules of interaction. They tend to dominate conversations by talking too much and fail to understand when the other person may want to speak. They also appear to miss the nonverbal cues that signal a listener's reactions.

Patients with RH damage within the posterior inferior frontal cortex (a site mirroring Broca's area in the left hemisphere) may present with a specific pragmatic impairment: aprosodia. The inability of aprosodic patients to vary the intonation of their speech is independent of their semantic knowledge of emotion (e.g. what sadness is) or their current mood. Thus an aprosodic patient's flat, monotonous speech does not indicate a lack of social awareness or muted affective responding. The notion that prosodic and other communication rules are independent of affective experience is consistent with the ability of psychopaths to learn these rules despite an apparent inability to experience the affective correlates of social bonding (e.g., interpersonal warmth). There is some evidence that this affective experience relies on the normal functioning of subcortical areas including the amygdala.

Experiencing social affect

As discussed above, successful interactions necessitate knowing the rules of what is appropriate to say and do and knowing when and how to apply these rules. However, knowing and abiding by these rules is not sufficient for the kind of meaningful social interactions that predict long-term relationships. These interactions depend not only on knowing the rules but experiencing and expressing the appropriate affect. Such a dissociation is highlighted in psychopathic patients who master communication rules to the point of social manipulation, but appear to lack a commensurate normal affective experience. Ted Bundy, for example, was frequently described as charming yet appeared unable to experience the affect associated with social relationships. After being incarcerated for several murders he said: "I didn't know what made people want to be friends. I didn't know what made people attractive to one another." As noted earlier, psychopathy has been associated with hypo-activity in the amygdala.

Relatedly, recent research has linked the inhibition of amygdaloid activity in Parkinson's

disease (PD) to muted affective reactivity. As PD is believed to be caused by a deficiency in dopamine, this research suggests that the hypo-activity of the amygdala and its associated muted affective reactivity stems from faulty dopaminergic gating. Although the exact mechanism is unknown, such faulty gating may impair the amygdala's role in social conditioning; the association of rewarding or aversive social stimuli with appropriate arousal.

III. Closing the loop: Social interaction

Like much of science, social neuroscience relies on patients, individual volunteers, and somewhat artificial paradigms in the attempt to isolate individual underlying mechanisms. But looking at the parts only provides so much information about the whole. Such an analysis may leave the reader wondering about how these individual processes interact with each other in more ecologically-valid contexts, namely real-life social interaction. That is, having stepped out of Nature, how does Science get back in again? To this end, researchers employ testing environments that evoke psychological processes that occur naturally, outside the laboratory. Ultimately, how the brain of an individual recognizes, understands and communicates with others is best studied in environments that incorporate the actual, or believed, presence of others. In these environments, social signals are decoded and responded to within a closed communication loop. Closing the loop creates the back-and-forth turn-taking that is the rhythm and tempo of natural communication. In addition, feedback from one's interaction partner shapes and directs the flow of that interaction. With such psychological realism in mind, a few innovative paradigms have begun to marry neuroscience methods with real or implied social interaction.

Interaction in fMRI: Trust games

Social interactions rely on everyone abiding by the same set of social rules. One such rule is reciprocity characterized by the quote “I’ll scratch your back if you scratch mine”. This social rule is so powerful and universal as to lead several psychologists to theorize that it confers a group-level evolutionary advantage by serving to detect and isolate “cheaters” who may exploit group members for personal gain. Behavioral economists have devised several games that elicit reciprocity in order to study cooperation and interpersonal trust within social interaction. Arguably the most well-known of these games is the prisoner’s dilemma.

The prisoner’s dilemma game was designed to mimic the real-world scenario in which police suspects are interrogated separately in the hopes that one would confess. Thus prisoner A and prisoner B are independently given the opportunity to testify against the other (“defect”) for the possibility of a reduced sentence (or, in the case of the game, a large sum of money). This reward is only good, however, if only one prisoner defects. In this scenario, the defector gets the large sum while his or her cooperative partner loses an equivalent amount. However, if both prisoners opt to defect, both lose a moderate sum of money. In the remaining possible outcome both prisoners “cooperate” (neither defects) and both win a moderate sum of money. In the iterated version of the game, both players repeatedly choose whether to cooperate or defect allowing participants to learn whether a partner is trustworthy as well as the opportunity to punish non-cooperative play. It is this iterated version that is arguably the most relevant to normal interactions and relationships.

In an initial fMRI study, investigators used the iterated version to examine the neural correlates of real-time interpersonal cooperation and trust. Participants were led to believe that they were playing against a fellow human participant or a computer program. When participants cooperated with their partners, greater activity was observed in mesolimbic areas (nucleus

accumbens (Nacc), caudate, mPFC and anterior cingulate) compared to outcomes elicited by all other strategies. Moreover NAcc, an area associated with reward, was sustained with repeated cooperation. These patterns of activity were similar, albeit less robust, when participants believed they were playing against a computer compared to another person. Thus reciprocal cooperation appears to engage areas associated with reward and this association is strongest during believed “real” (human-human) social interaction.

Trust games have also revealed that the drive to reciprocate need not involve cooperation. In some cases, people will expend inordinate energy and resources to reciprocate defection even to the point of personal loss (i.e., revenge). In the Ultimatum Game (UG) a pair of subjects has to agree on the division of a fixed sum of money. One participant in the pair, the “Proposer” is given the job of deciding how to divide the amount while the second participant, the “Responder” decides whether to accept or reject the proposed division. In the case of rejection, both receive nothing; in the case of acceptance, the proposal is implemented. Therefore, if the Responder were only interested in maximizing personal gain, he or she should accept all proposals regardless of how uneven. However, across hundreds of experiments, uneven divisions in which the Proposer gains the lion’s share (e.g., \$9 of \$10) are met with frequent rejection. The need to punish unfair behavior can outweigh simple monetary gain. Using a similar trust game, a study using PET found activity in the head of the caudate (just above the NAcc) when participants chose to punish selfish behavior.

Neuroimaging studies using trust games illustrate how interactive neuroscience methods can inform the study of social behavior. Although social behavior is complex, these findings suggest that relatively simple mechanisms such as reward anticipation may underpin a range of social phenomenon including cooperation, revenge, and the general adherence to social norms.

In addition, these findings suggest that the reward value of reciprocity is somewhat orthogonal to personal gain. In social interaction, what matters most is that everyone is playing by the same rules.

Interaction in fMRI: Social rejection

Consistent with the idea that social understanding builds upon more basic cognitive processes (e.g., reward), research on rejection suggests that overlapping neural systems may be involved in physical and social pain. In one study, participants were scanned during a game in which a virtual ball was tossed between players. In actuality, the “other players” were preprogrammed responses. At the beginning of the game, the ball was passed to the participant who could then pass it onto another player with a button press. After several trials in which the other players passed the ball to the participant, the participant stopped receiving tosses yielding unexpected social exclusion. Paralleling results from physical pain studies, the anterior cingulate cortex (ACC) was more active when participants were excluded from the game compared to when participants were included and this activity correlated positively with self-reported distress such as feeling ignored.

Future directions

While none of the studies we reviewed can make definitive claims about how the brain subserves social interaction, they suggest two important points. First, social understanding and social behavior emerge from, and are built upon, a more basic neural foundation. Brain regions engaged, for example, when detecting and perceiving animacy are also engaged when evaluating the intentions of others. Second, while relatively specific cognitive processes underlie much of our social behavior, these processes were likely driven to heightened sophistication by the complexities of social living. As this complexity may have driven cognitive function, it

behooves research to examine this influence. In this regard, pragmatic constraints of neuroimaging are not insurmountable for the investigation of social behavior. The employment of increasingly innovative paradigms will afford continued examination of social processes within their natural occurring context: interaction with others. Future research would benefit from considering individuals, whether patients or healthy volunteers, not as isolated units but as active inhabitants of an influential and affecting social world.

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Figure 1

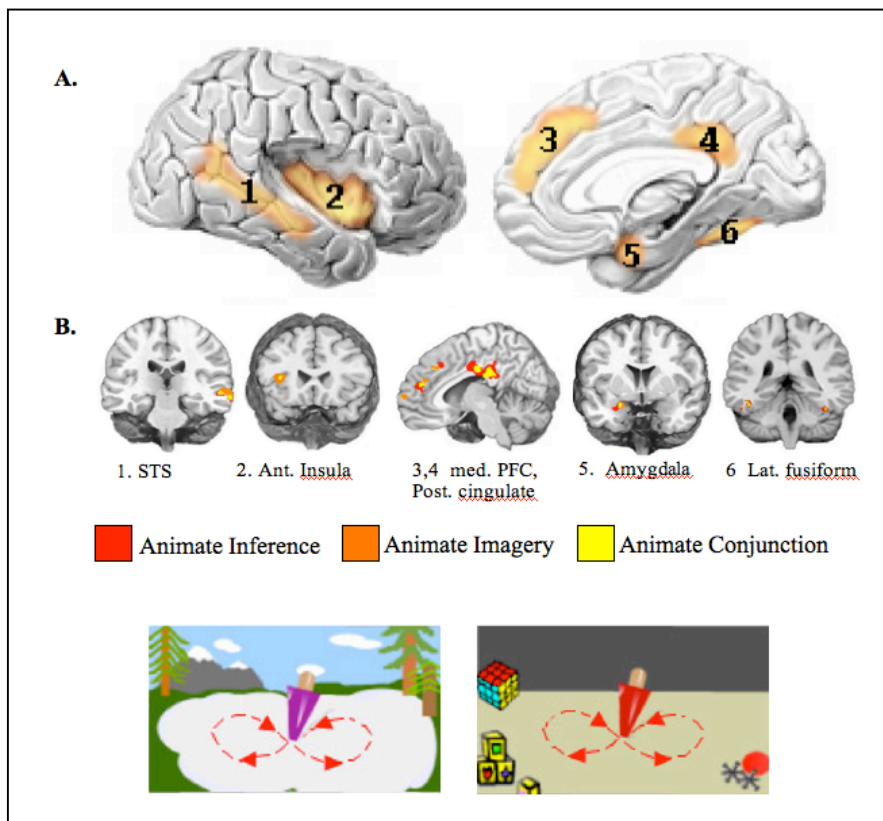


Figure 2

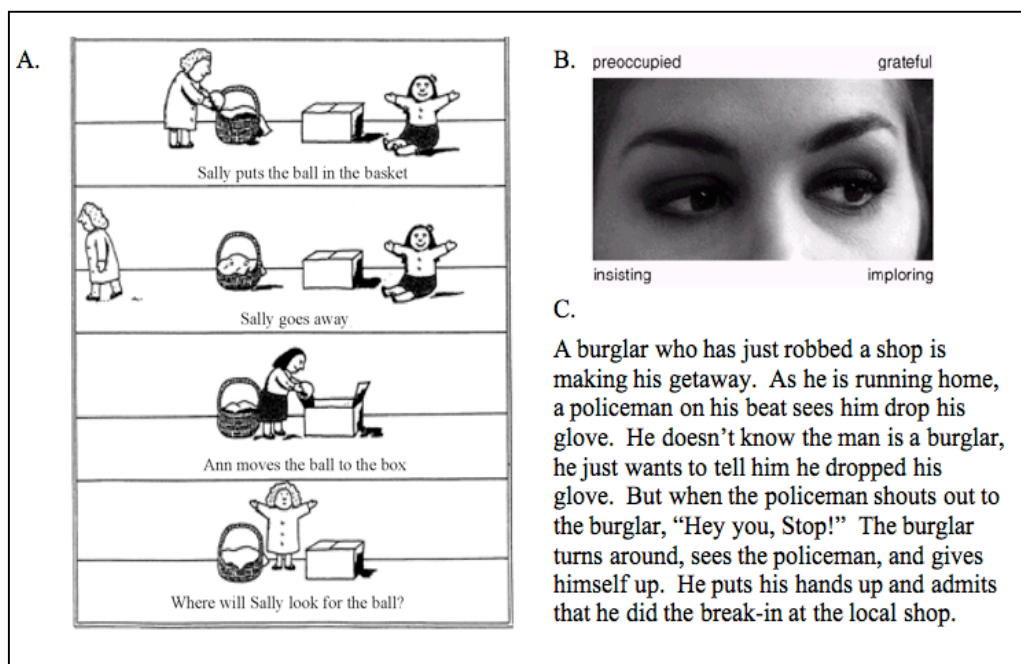


Figure 3

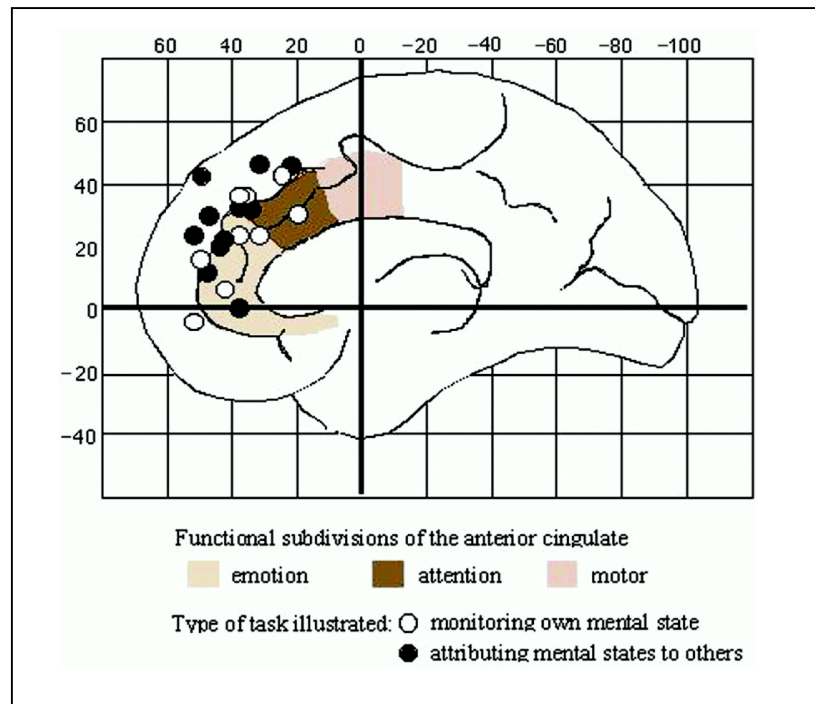


Figure 4

